topical administration as presently claimed, but this is not the only shortcoming of the reference. Significantly, Duckett teaches that it is the combination of L-arginine, ginseng, and Zizyphi fructus together that generates enough NO to have an effect on muscle relaxation. Column 4, lines 12-16, state that NO generation from L-arginine alone "would be insufficient to produce the desired result". In contrast, the present methods claim administration of an effective amount of L-arginine or a derivative thereof; "effective amount" is defined in the specification as being enough to bring about the desired amount of blood flow to the erectile tissue (see page 7, lines 7-9). As taught in column 4, lines 12-16 of Duckett et al. '824 does not teach using an effective amount of L-arginine effective to bring about the desired blood flow, because he teaches that L-arginine alone cannot be used to bring about the desired amount of blood flow to the erectile tissue. The Office Action further states that ginseng is an antioxidant, in support of the citation to Duckett et al. '824 in the rejection. Ginseng is not taught as an antioxidant in the Duckett et al. '824 composition, however, which the Office Action concedes (Office Action page 4). Rather, ginseng is taught as a necessary component of a three membered synergistic blend that causes NO stimulation. Moreover, ginseng is not an antioxidant within the present invention. An antioxidant, according to the present invention, converts superoxide molecules to hydrogen peroxide and oxygen, and is used in an amount that minimizes peroxynitrite damage caused by L-arginine (or derivatives thereof). (See page 6, lines 15-17; page 7, lines 6-9.) Ginseng does not convert superoxide molecules to hydrogen peroxide and oxygen and therefore is not an antioxidant within the present invention.

Hechtman '753 is cited to allegedly overcome the shortcomings of Duckett et al. '824. Duckett et al. '824 teaches oral administration, and Hechtman '753 teaches topical administration. Due to the significant differences in oral administration versus topical administration, one skilled in the art would not combine the teachings of the Hechtman '753 and Duckett et al. '824 references. Hechtman '753 teaches topical administration of L-arginine without antioxidant, to the anus. Thus, Hechtman '753 does not teach administration of a compound that protects against peroxynitrite damage. Moreover, that L-arginine may relieve hemorrhoidal pain and relax involuntary sphincter tension, according to Hechtman '753, does not mean it would enhance blood flow to erectile tissue.

Wysor '002 is cited as teaching administration of prostaglandin to enhance female sexual response. Prostaglandins are fat soluble and may cause transient stimulation, but

their half life is too short for them to be effective in the manner of the present composition, comprising L-arginine or derivatives thereof.

The Office Action concludes that it would have been obvious to topically apply the compositions of Duckett et al. '824, based upon the teachings of Hechtman '753 and Wysor '002. For a combination of references to be properly applied, there must be some suggestion of combination in the references themselves. Applicants respectfully submit such motivation is clearly lacking here. Duckett et al. '824 does not teach or remotely suggest topical application of their formulation. Hechtman '753 teaches topical application of a different formulation to a different body part to achieve a different ultimate result (i.e., relieving involuntary spasms versus engorgement of erectile tissue). Wysor '002 simply wouldn't work, despite its alleged teaching to the contrary (notably lacking examples demonstrating its efficacy). Even if the references were combinable in the manner suggested in the Office Action, which Applicants do not concede, the result would not be the present invention. None of the references teach the use of effective amounts of L-arginine (or derivatives thereof) and an antioxidant. The Office Action concedes that Duckett et al. '824, the primary reference, fails to teach an antioxidant, and neither of the secondary references are said to overcome this failure.

Claims 13-15 are further rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Duckett et al. '824 in combination with Hechtman '753, by itself or in further combination with Wysor '002 and further in view of Chobanian et al '847. This rejection is respectfully traversed.

The comments made above regarding Duckett et al. '824, Hechtman '753, and Wysor '002 apply equally here. The citation to Chobanian et al. '847 does not overcome the shortcomings of these references.

The Office Action concedes Duckett et al. '824, Hechtman '753 and Wysor '002 fail to "explicitly" teach an antioxidant, but cites to Chobanian et al. '847 as allegedly teaching various antioxidants in the treatment of fibrosis. More specifically, Chobanian et al. '847 is said to teach the combination of an NO stimulator together with an NO catabolism inhibitor. Chobanian et al '847 does not appear to teach L-arginine or its derivatives as NO stimulators. In any event, NO donors, NO synthase stimulators, and NO catabolism inhibitors are all taught as agents that stimulate NO. It would have been obvious, according to the Office Action, to have used an NO catabolism inhibitor, such as an antioxidant, in combination with the

L-arginine of Duckett et al. '824. As noted above, Duckett et al. '824 teaches the synergy of three ingredients in their compound. There is no teaching or suggestion whatsoever that additional compounds could be included in this synergistic blend, regardless of whether their effect is synergistic or "at least additive". Furthermore, antioxidants are taught by Chobanian et al. '847 as being NO catabolism inhibitors, not as protecting against peroxynitrite damage. Thus, neither of the references teach or suggest the protection of tissue from oxidative damage, as presently claimed.

In view of the foregoing remarks, it is submitted that Claims 1-25 are patentable over the prior art of record. Accordingly, an early Notice of Allowance of this application is respectfully requested.

In the event that any outstanding matters remain in connection with this application, the Examiner is invited to telephone the undersigned at (412) 263-4340 to discuss such matters.

Respectfully submitted,

Alan G. Towner
Registration No. 32,949
Pietragallo, Bosick & Gordon
One Oxford Centre, 38th Floor
301 Grant Street
Pittsburgh, PA 15219
Attorney for Applicants

(412) 263-4340